What is claimed is:

1. A high density output array of multiple yeast strains, wherein each resulting yeast strain in the output array contains at least two resulting genetic alterations, and wherein the resulting genetic alterations are different in each resulting yeast strain, the output array being the mating product of at least two input arrays, wherein at least one of the input arrays comprises multiple starting strains of yeast, wherein each starting yeast strain carries at least one genetic alteration, with the genetic alteration being different in each starting yeast strain.

2. The output array of claim 1, wherein the resulting yeast strains are in the diploid state.

3. The output array of claim 1, wherein the resulting yeast strains are in the haploid state.

4. The input or output array of claim 1, wherein the starting and resulting yeast strains are selected from any yeast strain that has two mating types and is capable of meiotic and mitotic reproduction.

5. The input or output array of claim 4, wherein the starting and resulting yeast strains are from either the *Saccharomyces cerevesiae* or the *Schizosaccharomyces pombe* species.

6. The input or output array of claim 1, wherein the yeast strains are located on plates, with between about 9 and about 6200 yeast colonies on one plate.

7. The output array of claim 1, wherein the resulting genetic alteration is a double mutant, the double mutant involving a mutation of two different endogenous yeast genes.

8. The output array of claim 7, wherein the double mutant carries the deletion of two different non-essential yeast genes.

9. The output array of claim 8, wherein the double mutant is either a synthetic lethal double mutant or a synthetic fitness double mutant.

10. The output array of claim 1, which comprises between about 1,000 and about 25 million resulting strains of yeast.

11. The input array of claim 1, wherein the starting genetic alteration in at least one starting yeast strain is selected from the group consisting of introduction of genes coding for an aptamer, introduction of a protein-protein interaction detection system, expression of a heterologous gene from a viral, prokaryotic, or eukaryotic genome, with the heterologous gene either having or not having a yeast homolog, transfection with a promoter operably linked to a reporter gene, and mutation or deletion of an endogenous yeast gene.

12. The input array of claim 11, wherein the aptamer is either a peptide aptamer or a nucleic acid aptamer.

13. The input array of claim 11, wherein the aptamer performs a function selected from the group consisting of inhibiting expression of a gene, increasing expression of a gene, inhibiting protein-protein interactions, enhancing protein-protein interactions, inhibiting the activity of a protein, and enhancing the activity of a protein.

14. The input array of claim 11, wherein the protein-protein interaction detection system is selected from the group consisting of a yeast two-hybrid system, the Ras recruitment system, the split ubiquitin system, and protein fragment complementation systems.

15. The input array of claim 11, wherein the heterologous gene is a human gene.

16. The input array of claim 15, wherein the human gene comprises a set of alleles, each differing by one or more SNPs.

17. A method for generating a high-density output array of resulting multiple yeast strains, wherein each resulting yeast strain carries at least two resulting genetic alterations, and wherein the resulting genetic alterations are different in each yeast strain, the method comprising:

a) generating multiple starting yeast strains, each strain carrying a starting genetic alteration;

b) mating sets of two starting yeast strains, wherein each of the two starting yeast strains contains a starting genetic alteration; and

c) recovering multiple diploid yeast strains which carry a resulting genetic alteration, wherein the resulting genetic alteration comprises the starting genetic alterations from each of the two mated starting yeast strains; and

d) arraying the genetically altered yeast strains in a high-density diploid output array.

18. A method for generating a high-density output array of resulting multiple yeast strains, wherein each resulting yeast strain carries at least two resulting genetic alterations, and wherein the resulting genetic alterations are different in each yeast strain, the method comprising:

a) generating multiple starting yeast strains, each strain carrying a starting genetic alteration;

b) mating sets of two starting yeast strains, wherein each of the two starting yeast strains contain a starting genetic alteration;

c) causing the mated strains to undergo sporulation, resulting in haploid strains;

d) germinating a single mating type;

e) growing the haploid spore progeny using selective growth criteria;

f) recovering multiple haploid yeast strains which carry a resulting genetic alteration, wherein the resulting genetic alteration comprises the starting genetic alterations from each of the two mated starting yeast strains; and

g) arraying the genetically altered yeast strains in a high-density format on an output array.

19. The method of claim 18, wherein the starting and resulting yeast strains are selected from any yeast strain that has two mating types and is capable of meiotic and mitotic reproduction.

20. The method of claim 19, wherein the starting and resulting yeast strains are from either the *Saccharomyces cerevesiae* or the *Schizosaccharomyces pombe* species.

21. The method of claim 18, wherein the starting and resulting yeast strains are located on plates, with between about 90 and 6200 yeast colonies on one plate.

22. The method of claim 18, wherein the resulting genetic alteration is a double mutant, the double mutant involving a mutation of two different endogenous yeast genes.

23. The method of claim 22, wherein the double mutant carries the deletion of two different non-essential yeast genes.

24. The method of claim 22, wherein the double mutant is either a synthetic lethal double mutant or a synthetic fitness double mutant.

25. The method of claim 18, wherein the output array comprises between about 1,000 and about 25 million resulting yeast strains.

26. The method of claim 18, wherein the starting genetic alteration in at least one starting yeast strain is selected from the group consisting of introduction of genes coding for expression of an aptamer, a protein-protein interaction detection system, expression of a heterologous gene from a viral, prokaryotic, or eukaryotic genome, with the heterologous gene either having or not having a yeast homolog, transfection with a promoter operably linked to a reporter gene, and mutation or deletion of an endogenous gene.

27. The method of claim 26, wherein the starting genetic alteration in both starting yeast strains is selected from the group consisting of introduction of genes coding for expression of an aptamer, a protein-protein interaction detection system, expression of a heterologous gene from a viral, prokaryotic, or eukaryotic genome, with the heterologous gene either having or not having a yeast homolog, transfection with a promoter operably linked to a reporter gene, and mutation or deletion of an endogenous gene.

28. The method of claim 26, wherein the aptamer is either a protein aptamer or a nucleic acid aptamer.

29. The method of claim 26, wherein the aptamer performs a function selected from the group consisting of inhibiting expression of a gene, increasing expression of a gene, inhibiting protein-protein interactions, enhancing protein-protein interactions, inhibiting the activity of a protein, and enhancing the activity of a protein.

30. The method of claim 26, wherein the protein-protein interaction detection system is selected from the group consisting of a yeast two-hybrid system, the Ras recruitment system, the split ubiquitin system, and protein fragment complementation systems.

31. The method of claim 26, wherein the heterologous gene is a human gene.

32. The method of claim 31, wherein the human gene comprises a set of alleles, each differing by one or more SNPs.

33. The method of claim 18, wherein the starting yeast strains carry selectable markers to permit efficient recovery of haploid spore progeny.

34. The method of claim 33, wherein the selectable markers are mating type specific promoters which permit selection of particular haploid mating types.

35. The method of claim 18, wherein robotic manipulation is utilized.

36. A method for conducting synthetic lethal analysis of yeast colonies within a high density array of multiple yeast strains, the method comprising:

a) generating a high-density output array of multiple yeast strains according to the method of claim 18;

b) comparing the phenotype of the haploid strains recovered in step f) of claim 18 to the phenotype of the starting yeast strains; and

c) detecting which haploid strains contain synthetic modulations by observing differences in the phenotype of the haploid strains as compared to the phenotype of the starting strains.

37. The method of claim 36, wherein the starting and resulting yeast strains are selected from any yeast strain that has two mating types and is capable of meiotic and mitotic reproduction.

38. The method of claim 37 wherein the starting and resulting yeast strains are from either the *Saccharomyces cerevesiae* or *Schizosaccharomyces pombe* species.

39. The method of claim 36, wherein the starting and resulting yeast strains are located on plates, with between about 90 and 6200 yeast colonies on one plate.

40. The method of claim 36, wherein the resulting genetic alteration is a double mutant, the double mutant including the mutation of two different endogenous yeast genes.

41. The method of claim 40, wherein the double mutant carries the deletion of two different non-essential yeast genes.

42. The method of claim 40, wherein the double mutant is either a synthetic lethal double mutant or a synthetic fitness double mutant.

43. The method of claim 36, wherein the output array comprises between about 1,000 and about 25 million resulting yeast strains.

44. The method of claim 36, wherein the starting genetic alteration in at least one starting yeast strain is selected from the group consisting of introduction of genes coding for expression of an aptamer, a protein-protein interaction detection system, expression of a heterologous gene from a viral, prokaryotic, or eukaryotic genome, with the heterologous gene either having or not having a yeast homolog, transfection with a promoter operably linked to a reporter gene, and mutation or deletion of an endogenous gene.

45. The method of claim 44, wherein the starting genetic alteration in both starting yeast strains is selected from the group consisting of introduction of genes coding for expression of an aptamer, a protein-protein interaction detection system, expression of a heterologous gene from a viral, prokaryotic, or eukaryotic genome, with the heterologous gene either having or not having a yeast homolog, transfection with a promoter operably linked to a reporter gene, and mutation or deletion of an endogenous gene.

46. The method of claim 44, wherein the aptamer is either a protein aptamer or a nucleic acid aptamer.

47. The method of claim 44, wherein the aptamer performs a function selected from the group consisting of inhibiting expression of a gene, increasing expression of a gene, inhibiting protein-protein interactions, enhancing protein-protein interactions, inhibiting the activity of a protein, and enhancing the activity of a protein.

48. The method of claim 44, wherein the protein-protein interaction detection system is selected from the group consisting of a yeast two-hybrid system, the Ras recruitment system, the split ubiquitin system, and protein fragment complementation systems.

49. The method of claim 44, wherein the heterologous gene is a human gene.

50. The method of claim 49, wherein the human gene comprises a set of alleles, each differing by one or more SNPs.

51. The method of claim 36, wherein the starting yeast strains carry selectable markers to permit efficient recovery of haploid spore progeny.

52. The method of claim 51, wherein the selectable markers are mating type specific promoters which permit selection of particular haploid mating types.

53. The method of claim 36, wherein robotic manipulation is utilized.

54. A method for assigning gene function by performing the synthetic lethal analysis of claim 36 to generate a synthetic lethal profile for a particular double mutant, and then performing cluster analysis of a set of synthetic lethal profiles to identify mutant alleles that result in similar compromised states with similar cellular functions perturbed.

55. The method of claim 36, wherein the synthetic modulation of the haploid strains is identified through the use of a genetic tag.

56. The method of claim 55, wherein the genetic tag is a unique 20mer oligonucleotide sequence.

57. A method for conducting synthetic lethal analysis of yeast colonies within a high density output array of multiple resulting yeast strains, the method comprising:

a) generating a high-density output array of multiple yeast strains according to the method of claim 17;

b) comparing the phenotype of the diploid strains recovered in step c) of claim 17 to the phenotype of the starting yeast strains;

c) detecting which diploid strains contain synthetic modulations by observing differences in the phenotype of the diploid resultant strains as compared to the phenotype of the starting strains.

58. A method for conducting small molecule screening of yeast colonies within a high density input array of multiple starting yeast strains, the method comprising:

a) generating multiple starting yeast strains in an input array, each strain carrying a starting genetic alteration;

b) exposing the starting strains in the input array to a biological effector; and

c) detecting which starting strains contain synthetic modulations by observing differences between the phenotype of the starting strains before and after exposure to the biological effector.

59. The method of claim 58 wherein the biological effector is a small molecule.

60. The method of claim 59, further comprising the step of screening for small molecules which kill yeast strains carrying a specified deletion mutation.

61. The method of claim 58, wherein the starting yeast strains are selected from any yeast strain that has two mating types and is capable of meiotic and mitotic reproduction..

62. The method of claim 61, wherein the starting yeast strains are from either the *Saccharomyces cerevesiae* or *Schizosaccharomyces pombe* species.

63. The method of claim 58, wherein the starting yeast strains are located on plates, with between about 90 and about 6200 yeast colonies on one plate.

64. The method of claim 58, wherein the starting genetic alteration in at least one starting yeast strain is selected from the group consisting of introduction of genes coding for expression of an aptamer, a protein-protein interaction detection system, expression of a heterologous gene from a viral, prokaryotic, or eukaryotic genome, with the heterologous gene either having or not having a yeast homolog, transfection with a promoter operably linked to a reporter gene, and mutation or deletion of an endogenous gene.

65. The method of claim 64, wherein the aptamer is either a protein aptamer or a nucleic acid aptamer.

66. The method of claim 64, wherein the aptamer performs a function selected from the group consisting of inhibiting expression of a gene, increasing expression of a gene, inhibiting protein-protein interactions, enhancing protein-protein interactions, inhibiting the activity of a protein, and enhancing the activity of a protein.

67. The method of claim 64, wherein the protein-protein interaction detection system is selected from the group consisting of a yeast two-hybrid system, the Ras recruitment system, the split ubiquitin system, and protein fragment complementation systems.

68. The method of claim 64, wherein the heterologous gene is a human gene.

69. The method of claim 68, wherein the human gene comprises a set of alleles, each differing by one or more SNPs.

70. The method of claim 68, wherein the starting yeast strains carry selectable markers to permit efficient recovery of haploid spore progeny.

71. The method of claim 70, wherein the selectable markers are mating type specific promoters which permit selection of particular haploid mating types.

72. The method of claim 58, wherein robotic manipulation is utilized.